Thermal Analysis as a tool in Materials Science

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Materials Science

- **Pharmaceutical materials science correlates physical properties of active compounds and pharmaceutical ingredients with the performance of the finished dosage product.**

- **Small molecules of pharmaceutical interest can exist in many different forms called morphs, which have different degrees of order at the atomic level.**

- **Detection, characterisation and quantification of amorphous, polymorphs and pseudo-polymorhs have been recent subjects of research globally.**

Thermal Analysis (TA)

- TA has been extensively used to provide insight into structural changes on molecular level.
- It is the most important analytical tool for studying physico-chemical properties of materials.
- Amongst the most widely used thermal analytical techniques are thermogravimetric analysis (TGA), differential scanning calorimetry (DSC) and hot stage microscopy (HSM).
- Recently, differential mechanical analysis (DMA) and thermally stimulated current (TSC) spectroscopy draw attention to a new ways of monitoring motions and changes in the structure of materials.

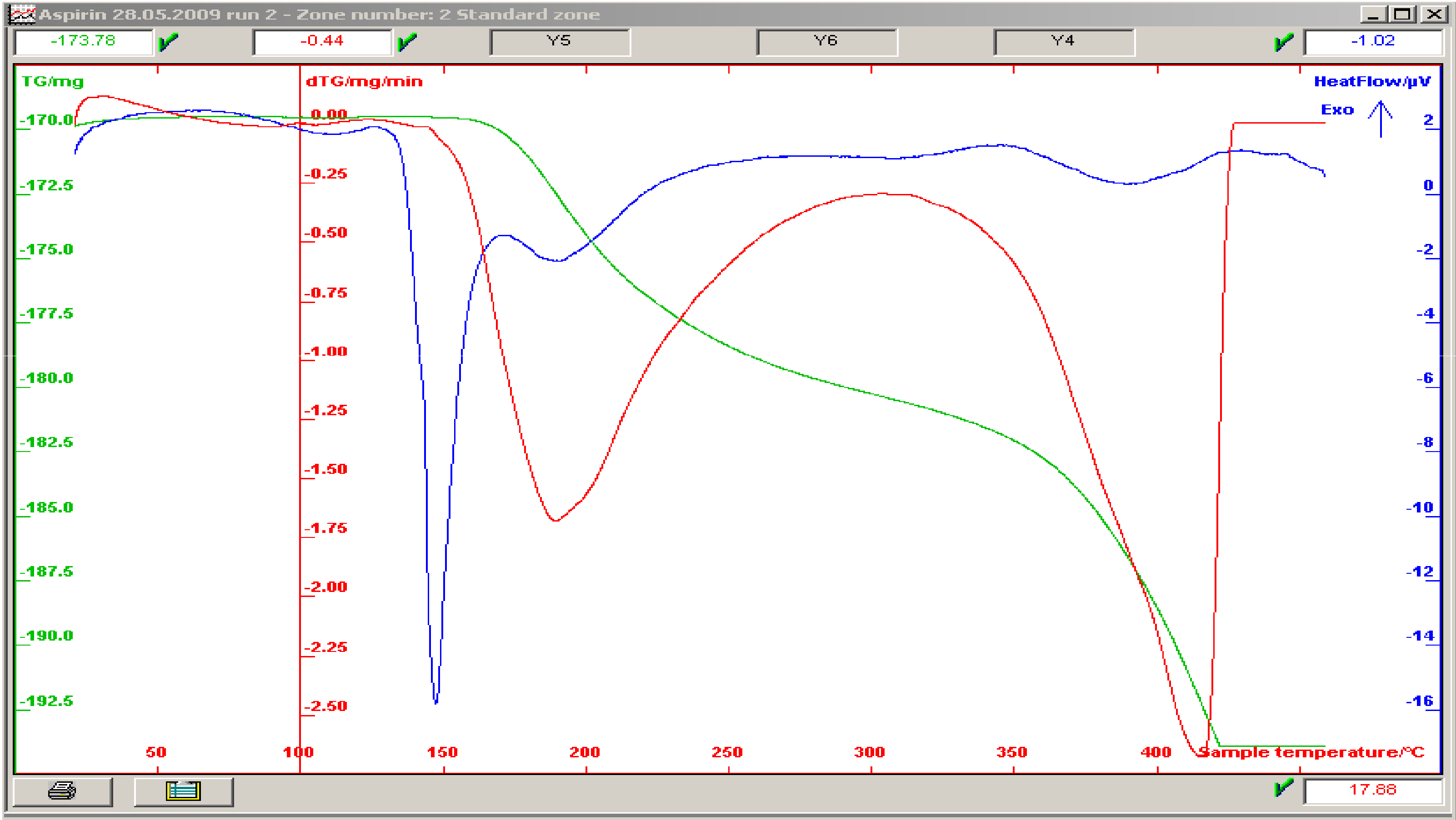
Thermogravimetric Analysis (TGA)

- water content
- solvent content
- oxidation
- degradation pathway
- decomposition
- stability

Thermogravimetric Analysis (TGA)

- **Hyphenated techniques:**
  - **TGA/DSC**
  - **TGA/IR**
  - **TGA/MS**
  - **TGA/DSC/IR**
  - **TGA/DSC/MS**

Thermogravimetric Analysis (TGA)



Hot Stage Microscopy (HSM)

- phase transitions
- softening
- crystalline habits
- size distribution
- stability

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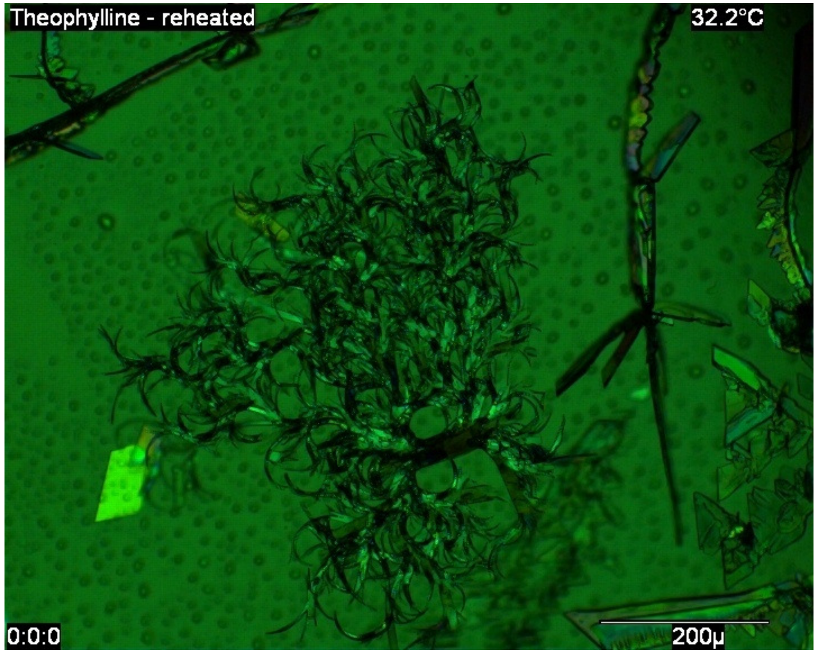
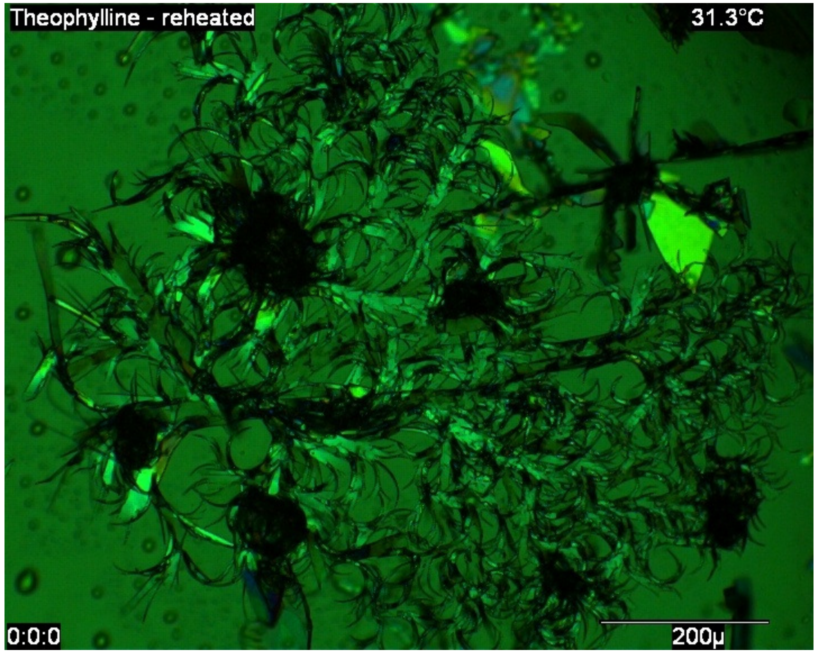
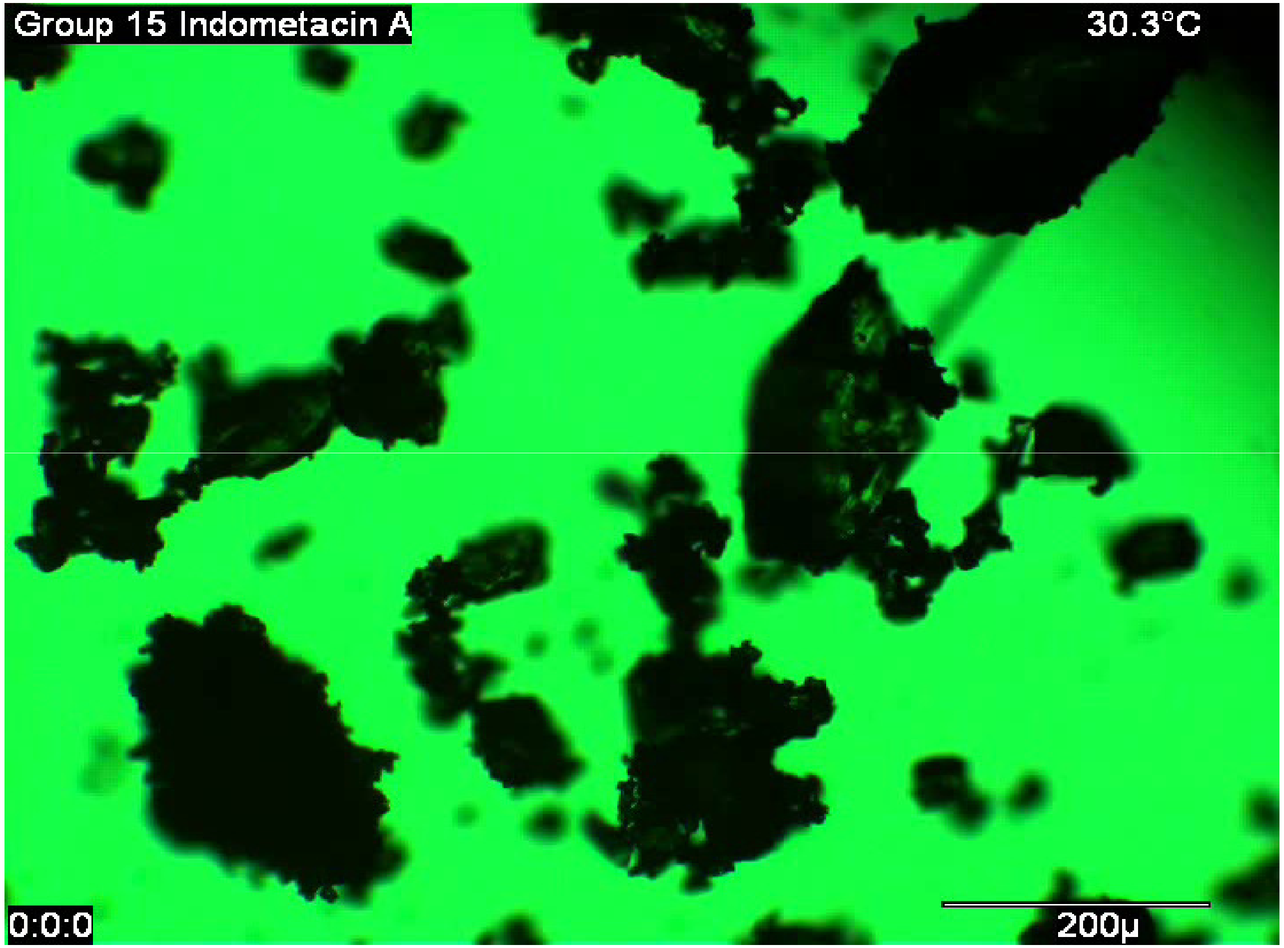
Hot Stage Microscopy (HSM)

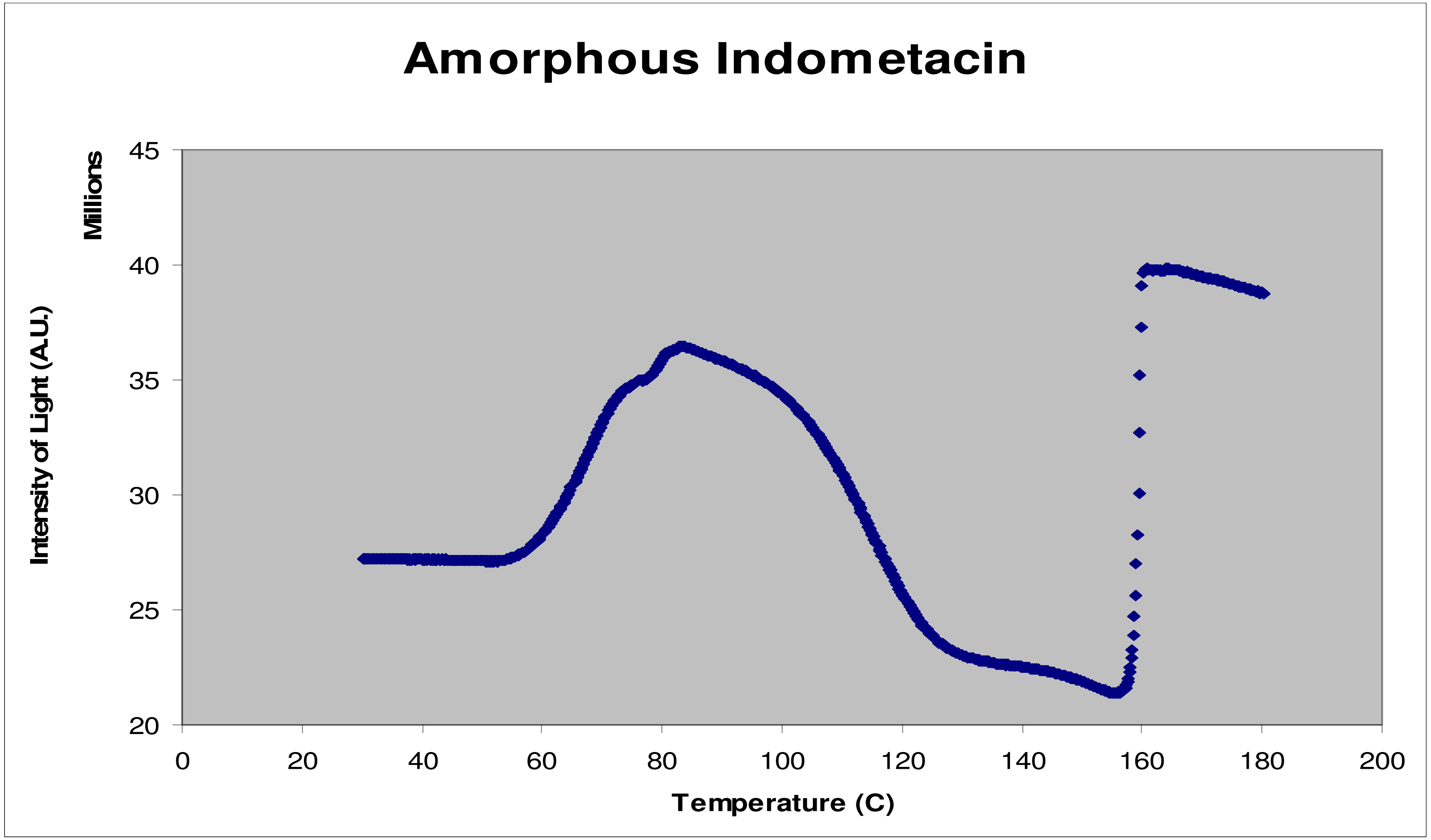




Amorphous Indometacin - HSM



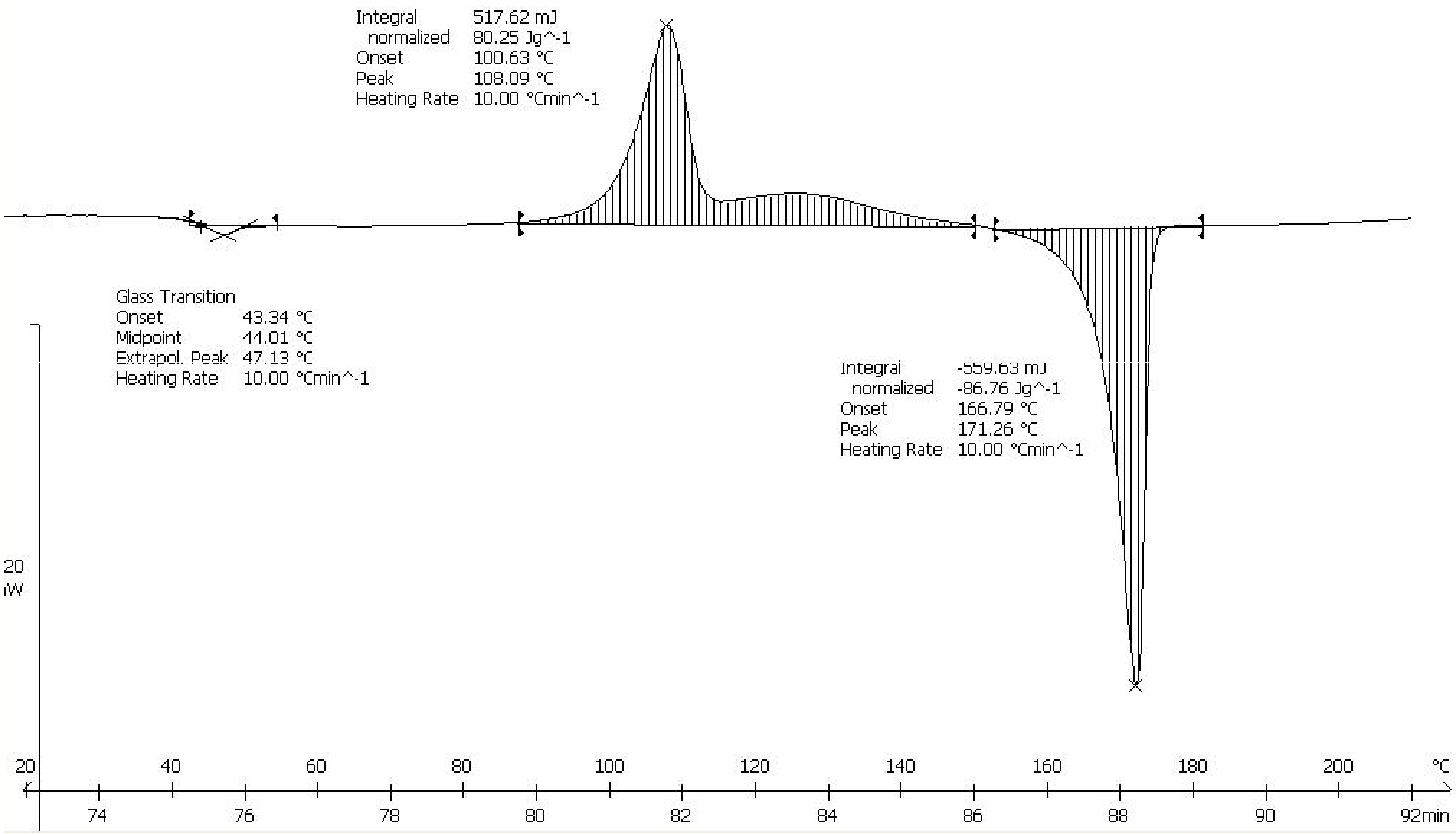
Amorphous Indometacin - HSM



Differential Scanning Calorimetry (DSC)

- 1st- and 2nd-order transitions
- glass transition, polymorphic transitions
- crystallisation, melting
- degradation
- identity, purity
- co-crystals, pseudo-polymorphs
- excipient compatibility, stability

Differential Scanning Calorimetry (DSC)



Thermally Stimulated Current Spectroscopy (TSC)

- α, β and γ transitions in materials
- molecular motions over a wide temperature range (-160ºC to 250ºC)
- cooperative and non-cooperative rearrangements
- relaxation map analysis
- calculation of activation energies for relaxation processes
- stability prediction, excipient compatibility

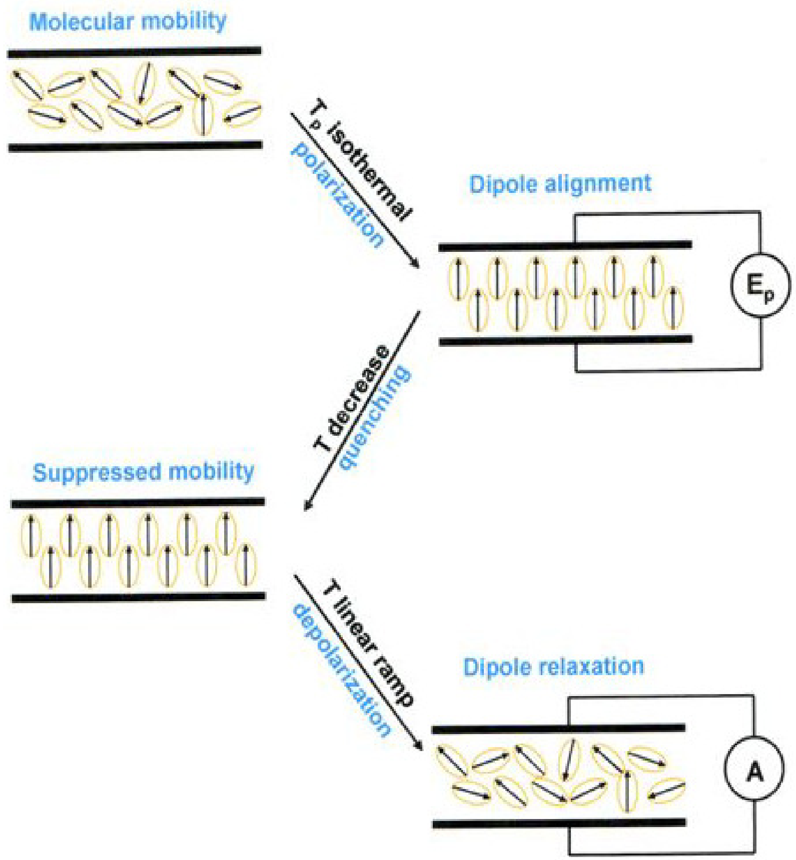
Thermally Stimulated Current Spectroscopy (TSC)

TSC is a general term applied to the measurement of current generated by temperature-activated relaxation of molecular dipoles in response to the application of a static electric field

- **1936, Frei and Grotzinger**

- **electrets, ionic crystals**
- **waxes, resins**
- **ceramics, plastic**

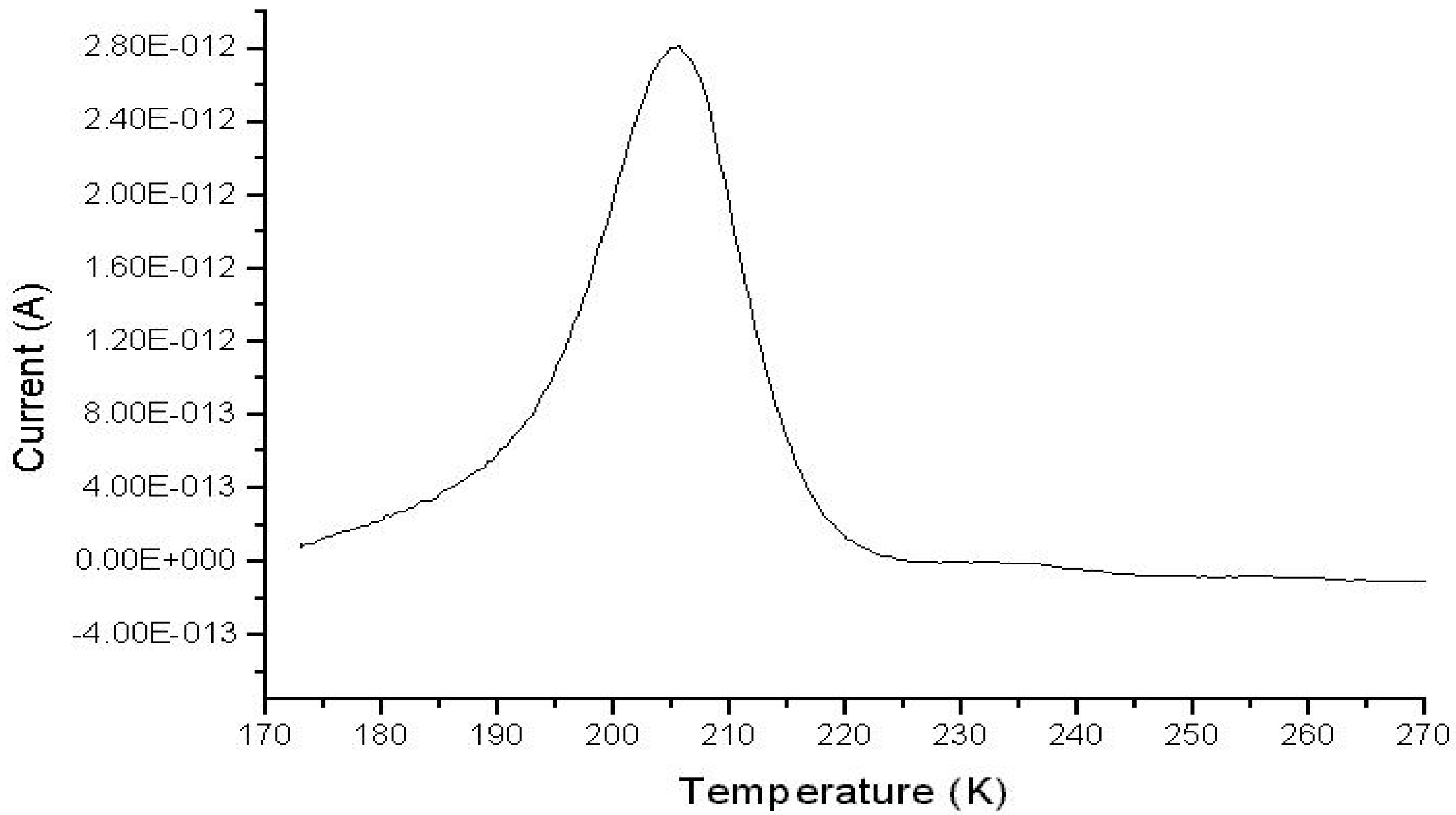
TSC origin



Experimental variables:

- Temperature of polarization
- Time of polarization
- Polarization field
- Cooling rate
- The lowest temperature
- Time at lowest temperature
- Heating rate
- Final temperature
- Temperature of stabilization

TSC spectrum



Main parts of the instrument

Thermostated sample holder

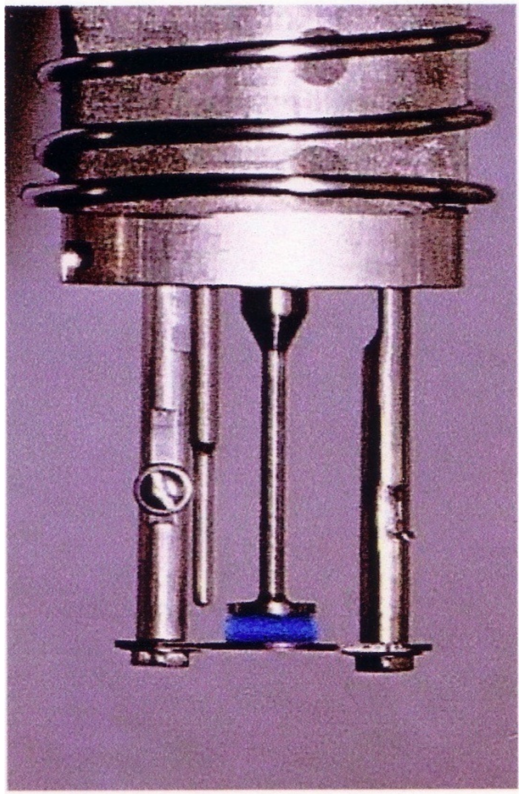
Vacuum system

Heating and Cooling unit

DC generator

Current detector (10^{-4} to 10^{-16} A)

Recording unit



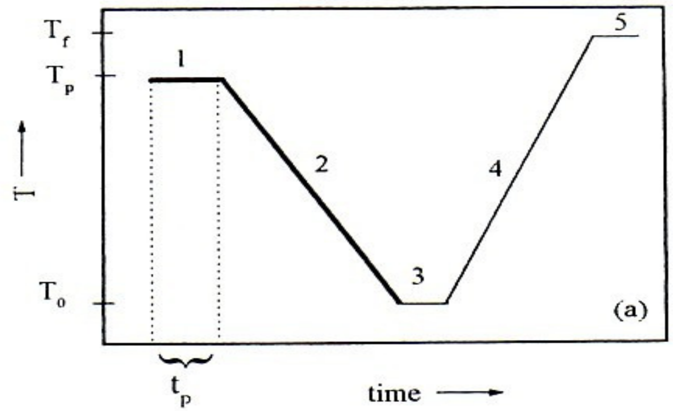
Amorphous Materials

Glass transition is characterised by:

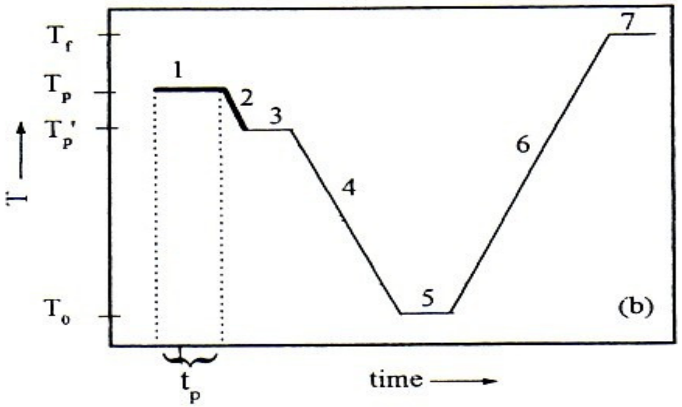
Heat capacity change (DSC)

Visco-elastic changes (TSC)

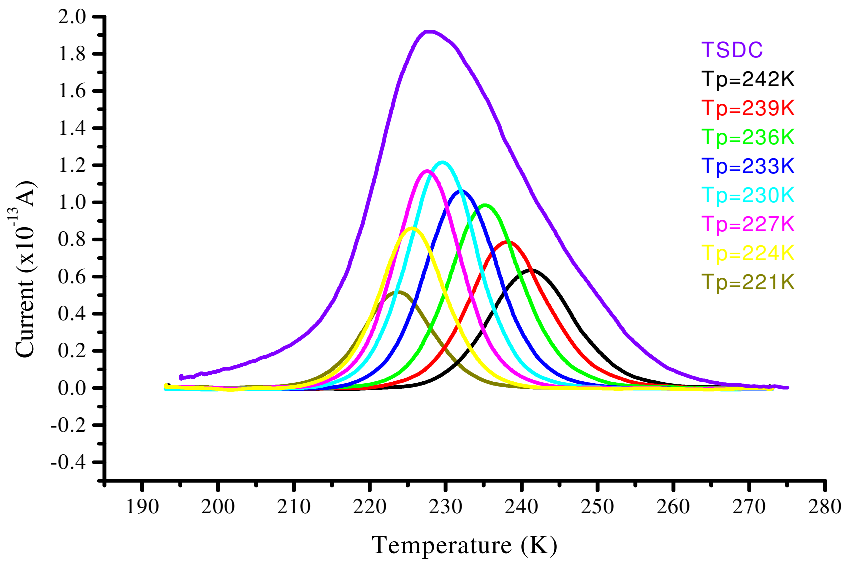
TW-TSDC



T
T_f
T_p
T_0
1
2
3
4
5
(a)
t_p
time

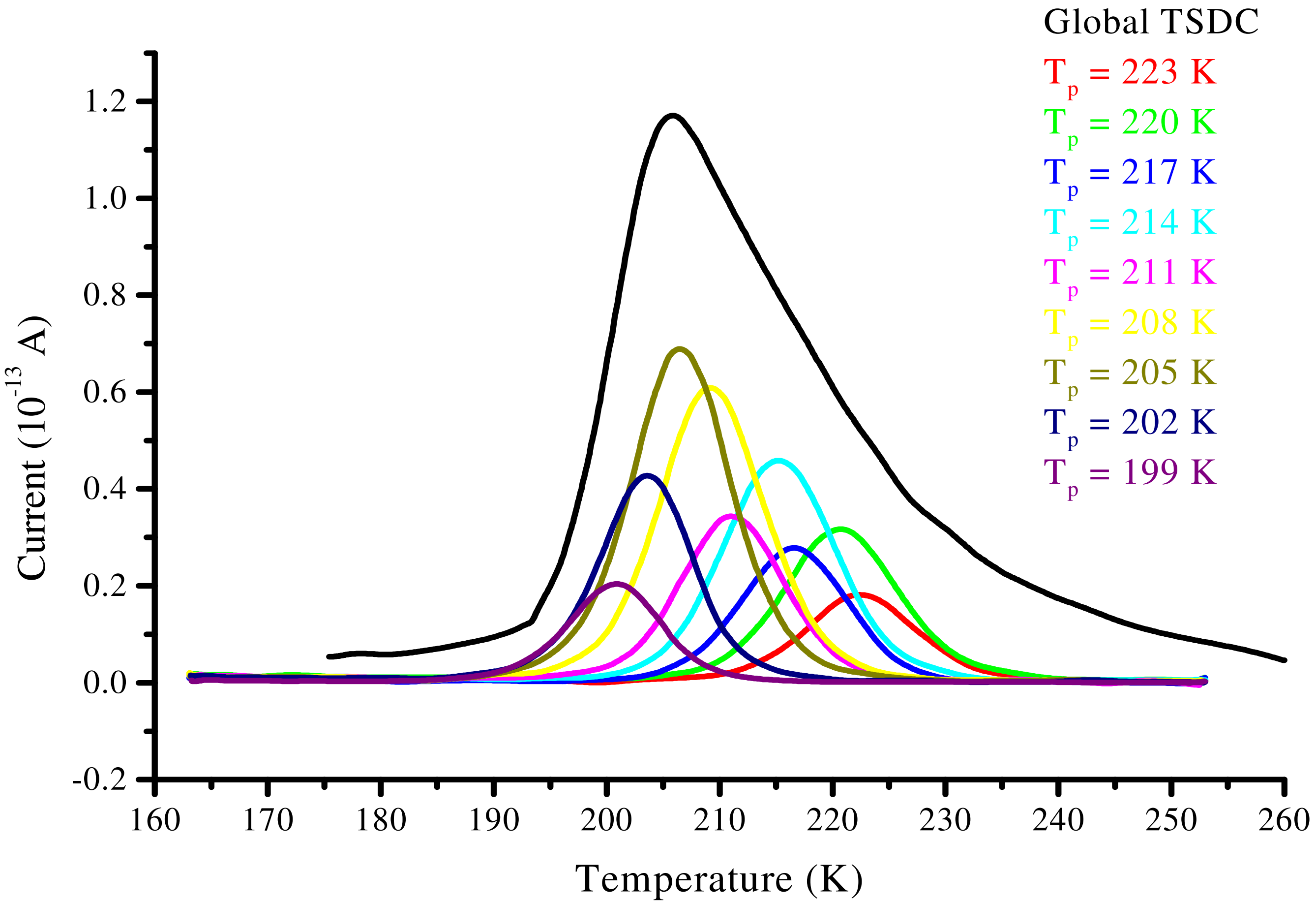


T
T_f
T_p
T_p'
T_0
1
2
3
4
5
6
7
(b)
t_p
time

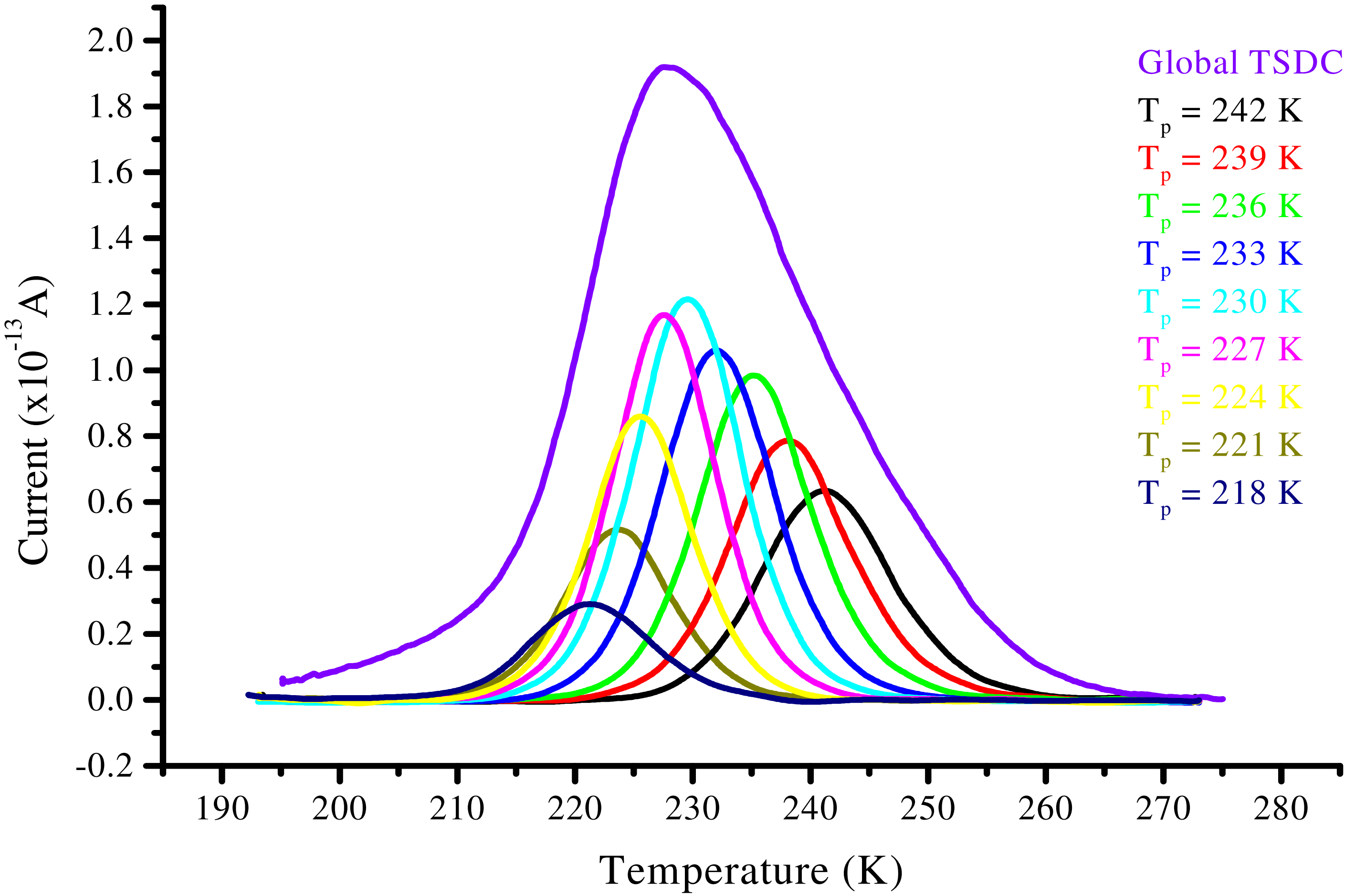


TSDC
Tp=242K
Tp=239K
Tp=236K
Tp=233K
Tp=230K
Tp=227K
Tp=224K
Tp=221K
Current (x10^-13 A)
Temperature (K)
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
190
200
210
220
230
240
250
260
270
280

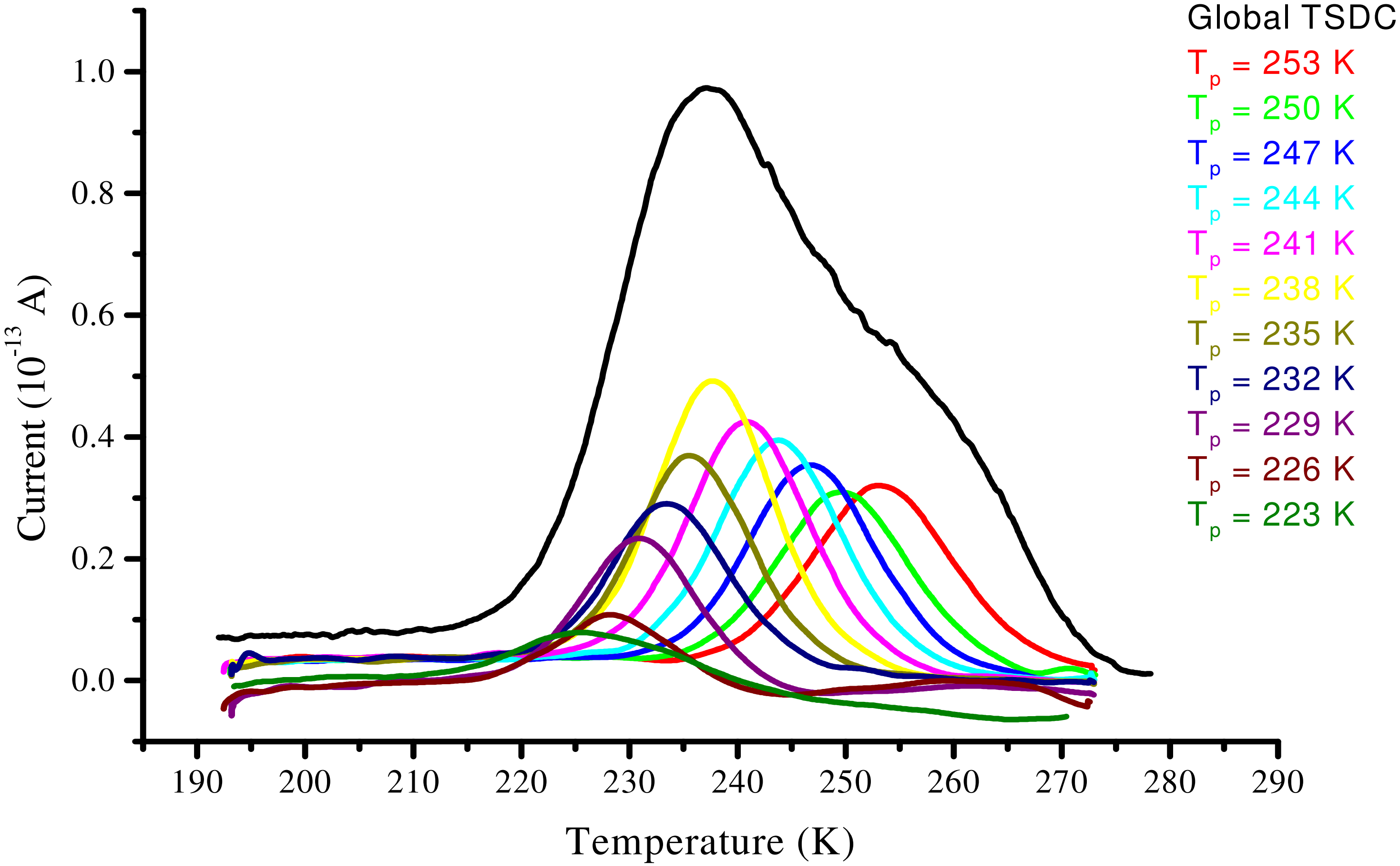
TSC PEG 4000 - Aldrich



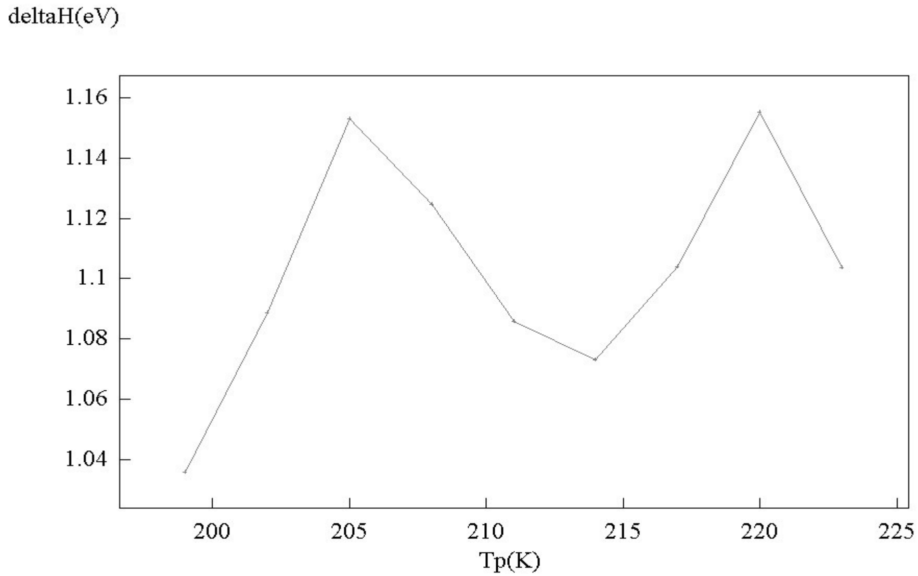
TSC PEG 6000 - BDH

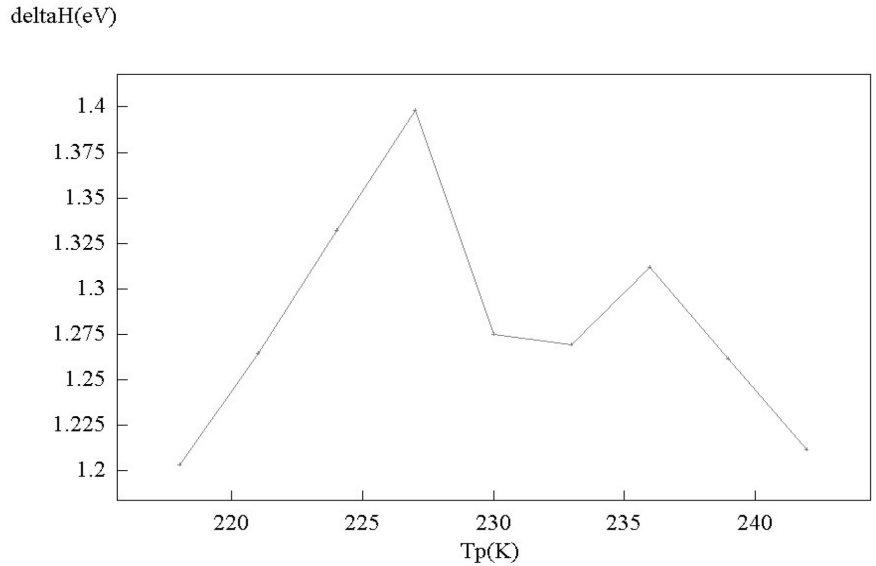


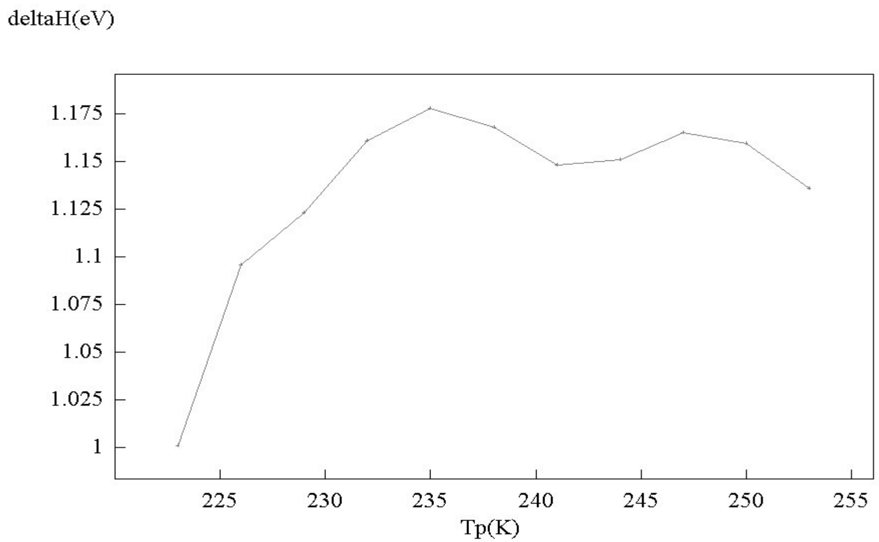
TSC PEG 20000 - Clariant



TSC PEG 4000/6000/20000







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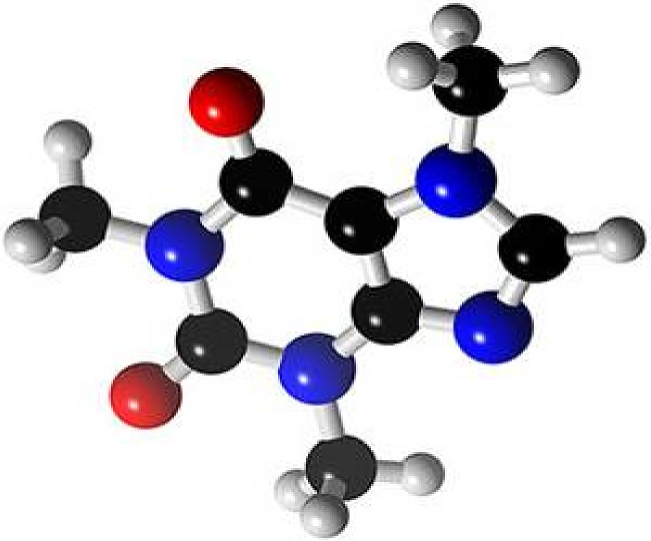
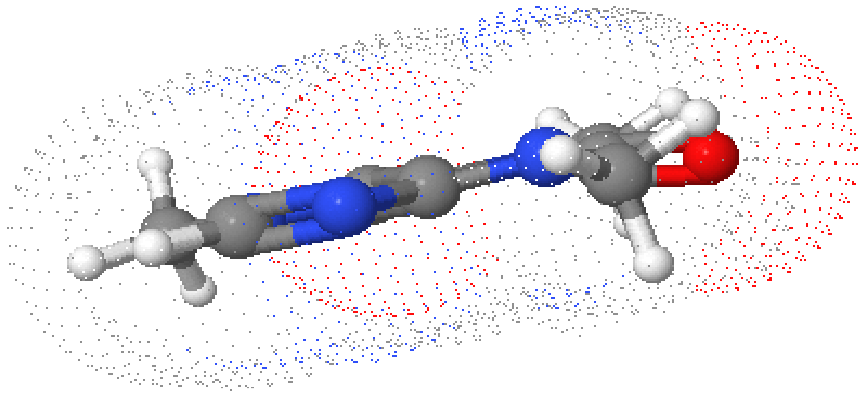
Caffeine





Polymorphic transition

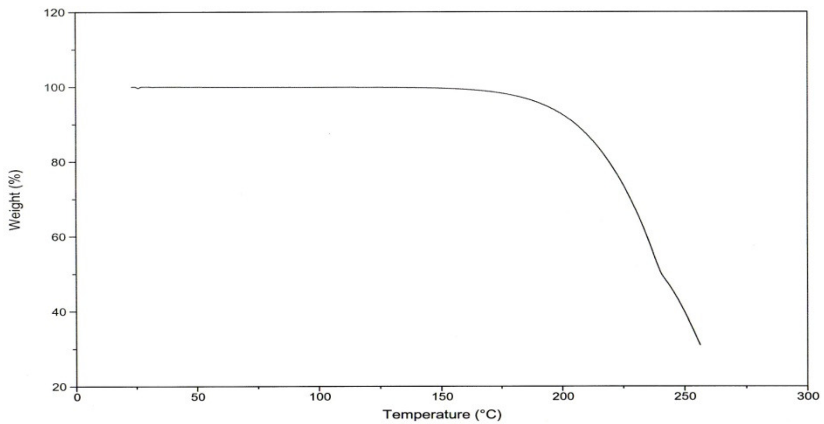
Form II is stable at room temperature

Form I is stable above 150°C

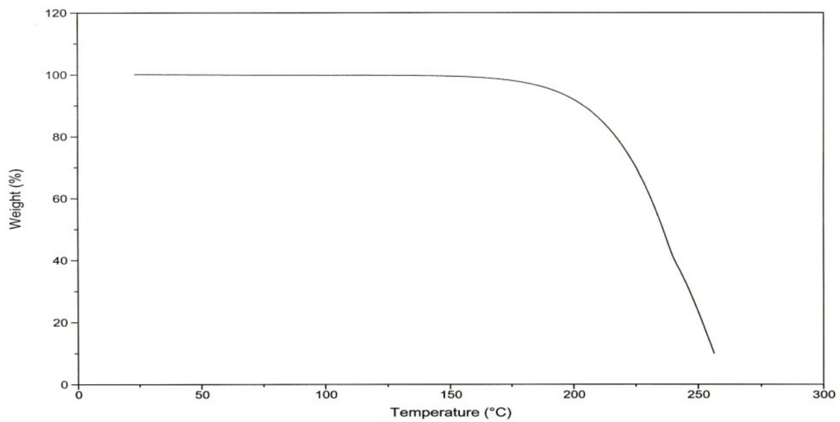
Xanthine alkaloid (theophylline, theobromine)

Caffeine - TGA Results

Form I



Form II



Both forms show no water content

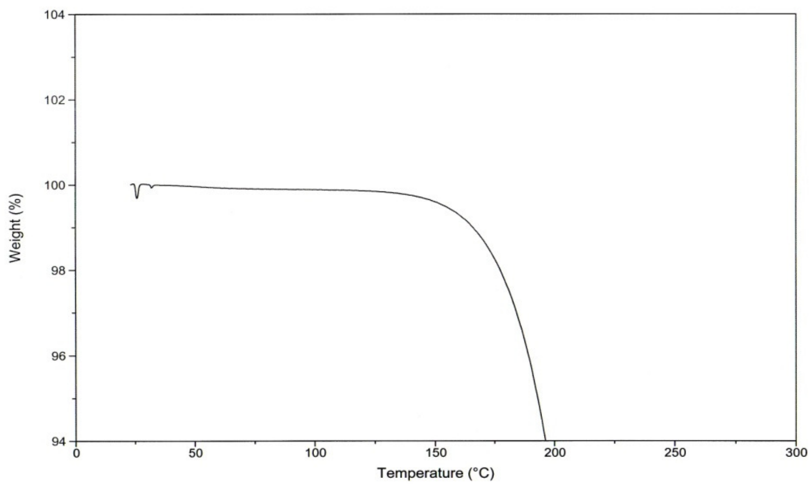
Dehydration of monohydrate occurs rapidly at 40°C

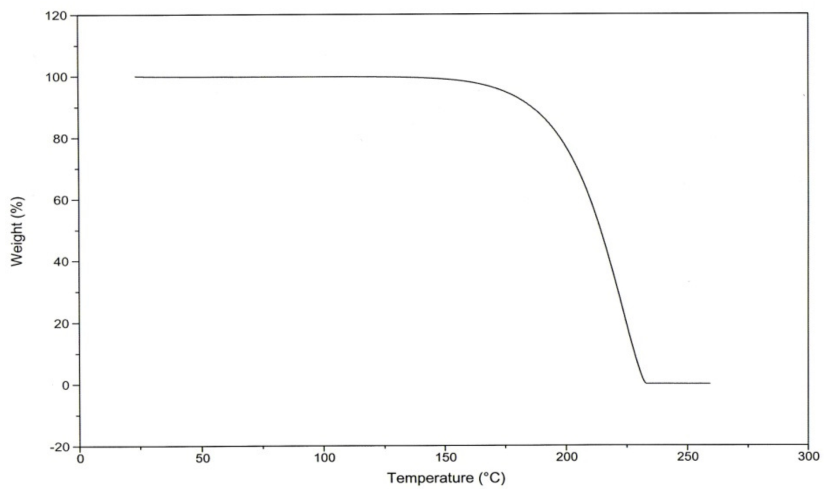
Melting point was observed at 240°C

(change in slope from –1.6%/ºC to –1.1%/ºC)

Caffeine - TGA Results

Heating rate: 10K/min | **2K/min**

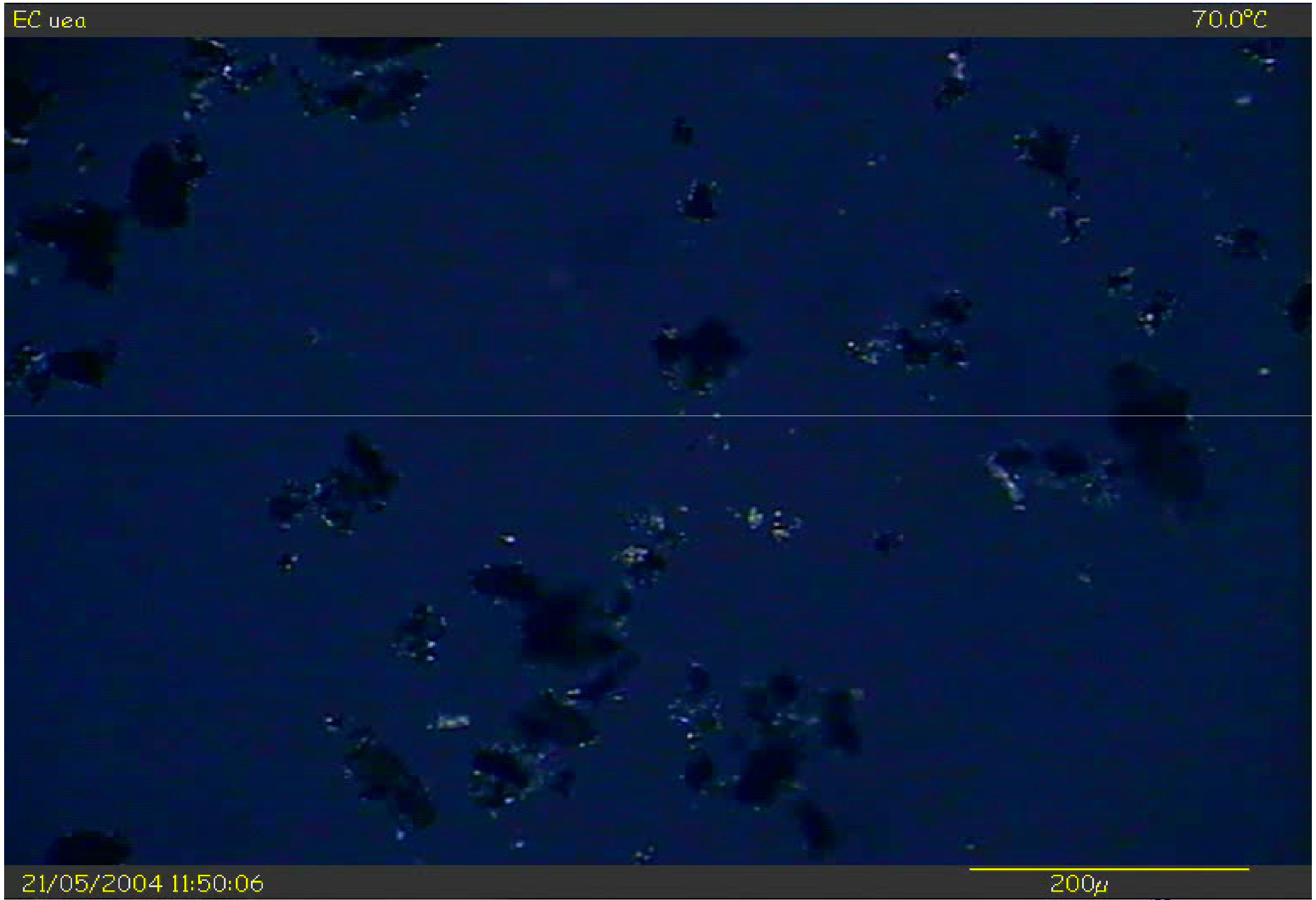




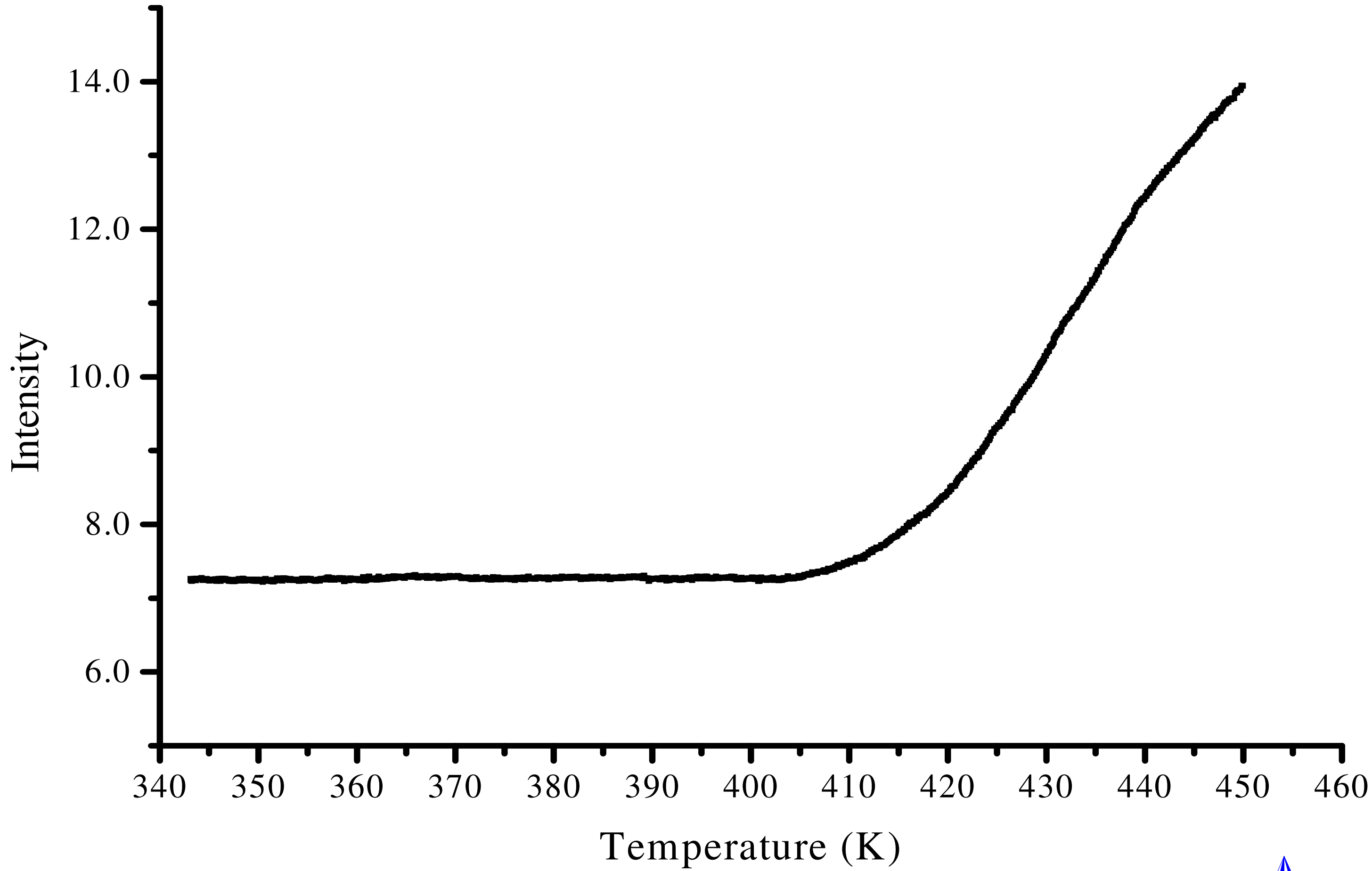
Above 160°C sublimation become a fast process

Faster heating ramp can prevent loss of the caffeine during the examination

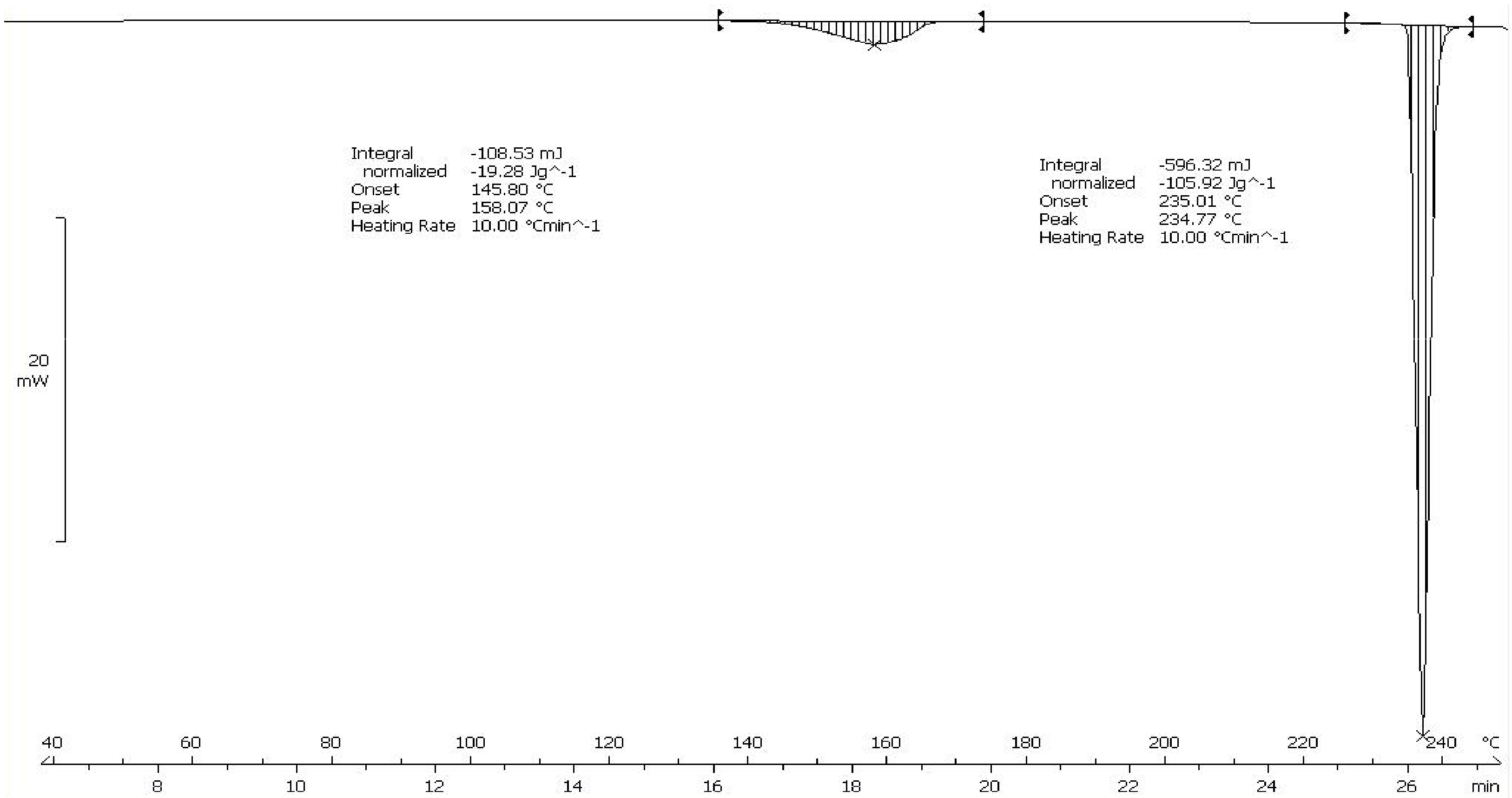
Caffeine - HSM



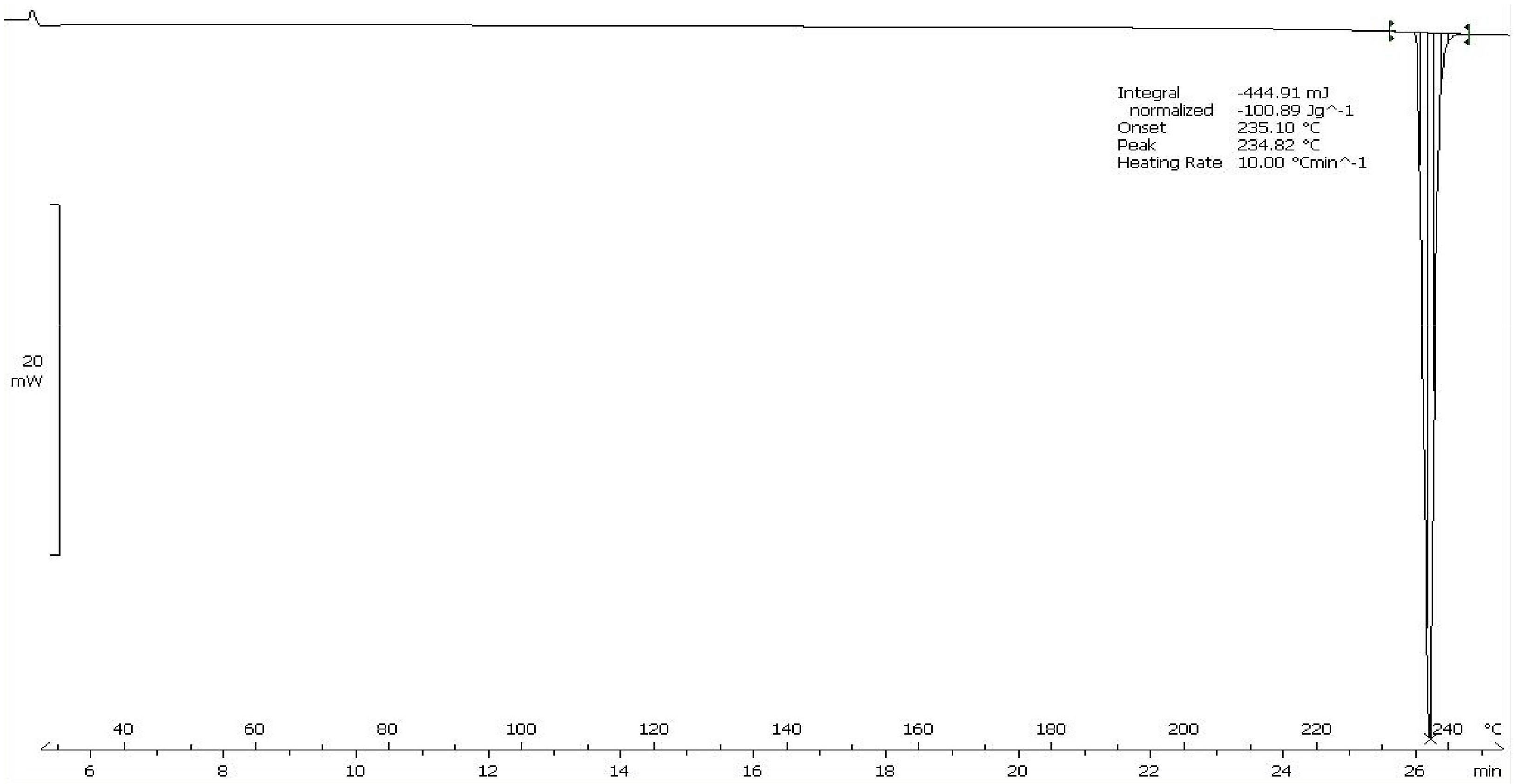
Caffeine - HSM results



Caffeine Form II – DSC Results

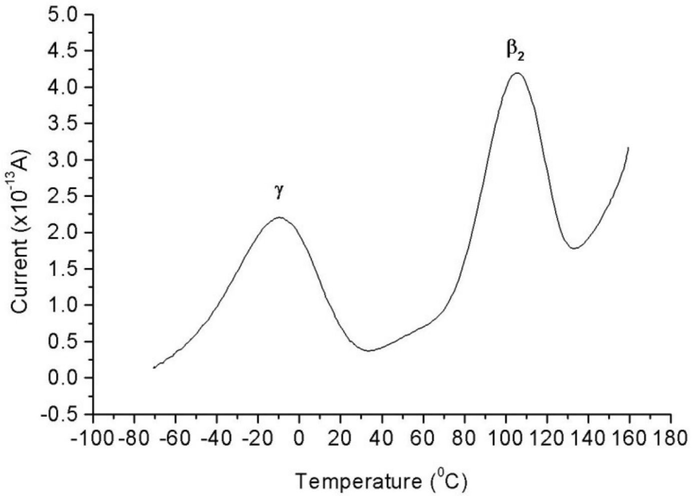


Caffeine Form I – DSC Results

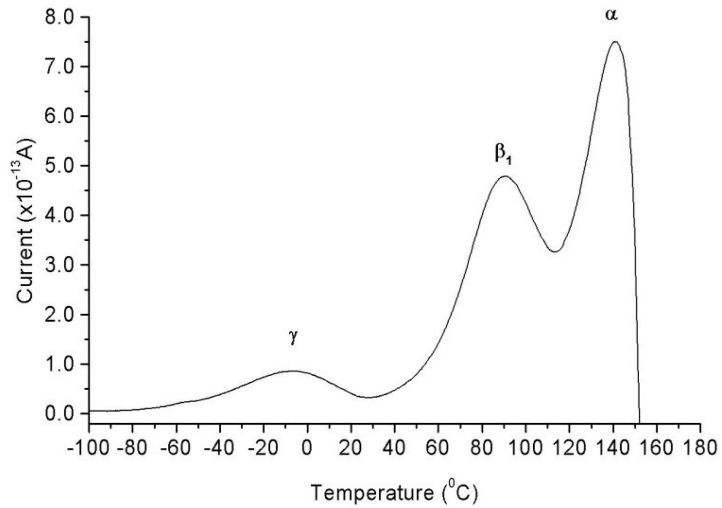


Caffeine - TSDC Results

Form I



Form II



α-process	139ºC	Form II only - *polymorphic transition*
γ-process	-8ºC	Forms I and II - *orientation of side group*
β_1-process	91ºC	Form II
β_2-process	107ºC	Form I - *orientation/mobility of sub-unit*

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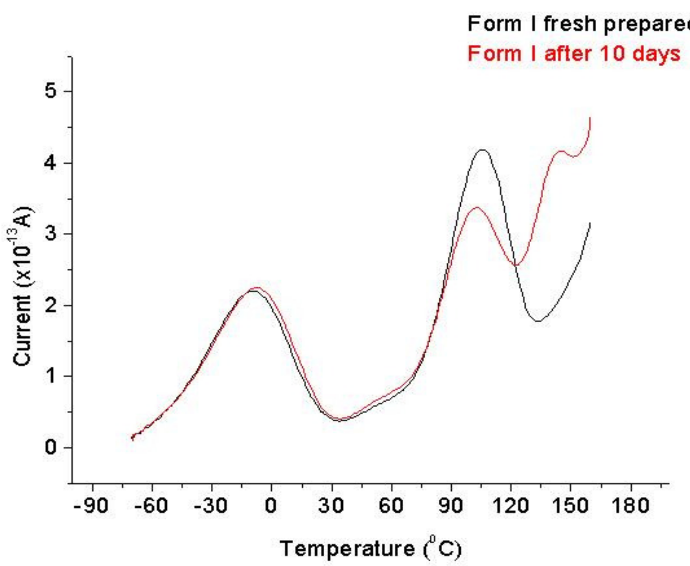
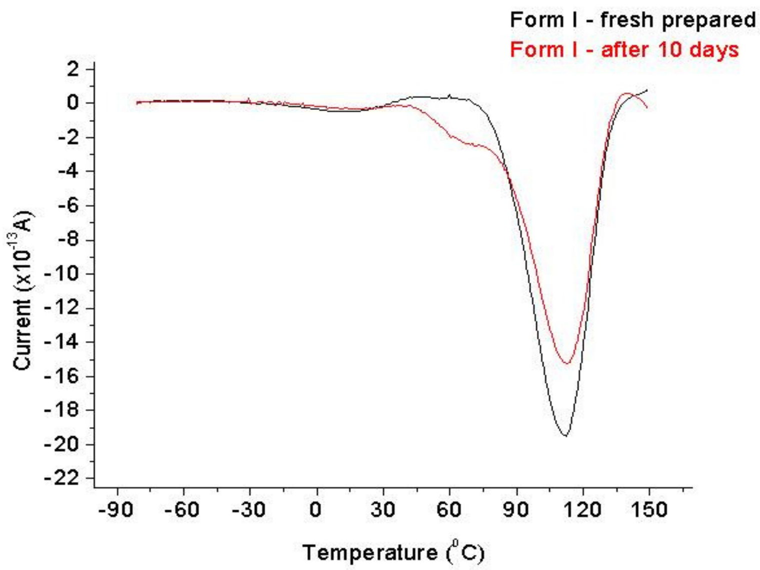
Kinetic Parameters - TSC Method

TSDC



SDC



Conclusions

- identity, purity
- water/solvent content
- amount of different amorphous and polymorphic form present
- co-crystals and pseudo-polymorphs
- secondary relaxations in materials (β and γ)
- calculation
- stability prediction, excipient compatibility

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